REMARKS

Claims 1-18 are under examination and all have been rejected.

Rejection Under 35 U.S.C. §103

Claims 1-4 and 8-18 were rejected under 35 U.S.C. 103(a) as unpatentable over Dorval (U.S. Pat. No. 5,561,045) in view of Cabilly et al (U.S. Pat. No. 4,816,567). The Examiner contends that it would have been obvious to one of ordinary skill in the art to modify the teaching of Dorval to include altered immunoglobulins of Cabilly et al that contain heavy and light chain variable regions.

However, the Examiner fails to explain the motivation for such combination and Applicant contends that there is none.

Cabilly teaches the production of chimeric antibodies, consisting of a variable region from one species, which is specific for antigen, and a constant heavy region from a different species, the latter being a potential recipient of the antibody. Thus, unwanted immunogenic reaction is avoided because the heavy chain region with the Fc binding site is from the recipient species. Thus, Cabilly et al solve a problem like the problem to be solved by Applicant but Applicant solves the problem by blocking the heavy chain constant region with Protein A rather than using a chimeric antibody (which must be prepared recombinantly).

The Examiner points out that because Applicant's invention claims a product, what this product is used for will not be given patentable weight. Applicant contends that this is certainly true for novelty issues but here the rejection is based on obviousness so that there is an admission that the product is not *per se* disclosed and the use may be relevant if it goes to the motivation to combine. Thus, if the teaching of one reference is

useless in the other, or results in a disadvantage, or fails to solve the problem Applicant is trying to solve, then there is no motivation to combine.

The Examiner notes that other embodiments of Cabilly were relied on in rejecting the claims but does not state what they are. Applicant can make no arguments concerning unnamed other embodiments. However, the Examiner also contends that Applicant's arguments are based on *in vivo* use whereas Cabilly also discloses an *in vitro* ELISA assay.

The ELISA of Figure 10 in Cabilly is described at column 26, lines 4 to 24, dealing with CEA as the antigen. In an ELISA, one binds an antigen to a plate, then applies an antibody specific for the antigen and then applies a second antibody specific for the first, thereby completing the "sandwich." However, the ELISA of Cabilly was not intended to detect an analyte but simply to demonstrate that the antibody was chimeric. Thus, Cabilly used CEA as the antigen, chimeric anti-CEA as the first antibody (with light and heavy chains of different species) and anti-IgG against the heavy chain species as the second antibody.

Nevertheless, the question is not whether two references can be combined but whether there is a motive to combine them. Dorval teaches antibodies useful in *in vitro* assays but for such assays any conventional monoclonal antibody will work. There is no reason to use the expensive recombinant antibodies of Cabilly because all antibodies have an Fc site that would bind protein A in the Dorval assay. In short, no one would think to use the Cabilly antibodies in the Dorsal assay for an analyte because chimeric antibodies have no value in such an assay. In fact, chimeric antibodies would be disadvantageous because, in addition to there being no adverse reaction to avoid, they are expensive and time consuming to make in that recombinant means are required. No one is going to think to make expensive recombinant antibodies just to run the assay of Dorval. That would be like using the space shuttle to fly from New York to Washington, D.C. – possible, but why would you do it given the cost and time for launch? To perform

the Dorval assay one only needs an antibody specific for the antigen and that will bind the protein A complex, i.e., any antibody specific for the antigen.

In addition, Dorval uses protein A, but protein A will bind to the constant heavy chain region of the first antibody (as admitted by Dorval at column 5, lines 41-43) and block binding of the Fc-specific second antibody. Cabilly produced chimeric antibodies to avoid reactions at the Fc region, just the region bound by Protein A, so Cabilly's chimeric antibodies afford no advantage in such procedures but, rather, are disadvantageous because of the cost and time in making them (and then only to frustrate their advantage by adding protein A). This is why Dorval had to come up with a new *in vitro* assay method – because the conventional ones will fail in the presence of Protein A (admitted by Dorval at column 2, lines 7-10, where he states that "the determination of any species in a sample using Protein A and a binding partner of the IgG class is complicated when performed according to known techniques", which techniques include ELISA).

In sum, there is no motivation to combine Dorval and Cabilly and, in fact, doing so would result in a disadvantage.

Claims 1 and 8-10 were rejected under 35 U.S.C. 103(a) as unpatentable over Sano (U.S. Pat. No. 5,665,539) in view of Cabilly et al (U.S. Pat. No. 4,816,567).

In response, Applicant again contends that there is no reason to combine them. This does not mean that they cannot be combined but the ability to combine, and the motivation to do so, are not the same thing and one cannot substitute for the other.

Sano teaches a means of detecting an antigen by binding an antibody to it wherein the antibody is attached to a DNA that can be amplified (i.e., detected) using the polymerase chain reaction and Protein A is taught as part of a complex to attach the DNA to the antibody. If combined with Cabilly, the chimeric antibody of Cabilly would be complexed with the DNA – but why use an expensive chimeric antibody that binds the detectable antigen no better than any other antibody. One would simply not look to

chimeric antibodies to achieve such a result.

Sano and Cabilly represent essentially different technologies. Thus, for example, employing the antibodies of Cabilly in the method of Sano achieves no better result than any other antibodies because the unique feature of Cabilly is having light and heavy chain regions from different species to avoid unwanted binding at the Fc site (located on the heavy chain). Sano discloses a method for detecting antibody binding to an antigen via PCR of a DNA attached to the heavy chain (through Protein A, which binds the Fc site). Again, what is the motivation to use Cabilly's expensive, time consuming to produce, recombinant chimeric antibodies (with an Fc portion from a different species than the portion that binds antigen) if you are just going to tie up that Fc portion with a Protein A complex that binds DNA. No one in the art would look to combine Cabilly with Sano because there is only disadvantage of time and money in using Cabilly's chimeric antibodies versus any other antibody with an Fc portion to attach DNA and a variable region specific for the antigen to be detected.

In sum, all one needs to do the assay taught by Dorval or by Sano is an antibody specific for the antigen to be detected and that will complex with Protein A (on the Fc portion – common to all antibody heavy chains regardless of what species they are from) and not the expensive recombinant chimerics taught by Cabilly for a very special use. Thus, there is no motivation, only disadvantage in time and money with no advantage in performance, to combine Cabilly with Sano or Dorval, and no one in the art would ever think to do that, even though such combination is technically achievable.

No fee is believed due in making this response. The Commissioner is authorized to charge payment of any additional filing fees required under 37 CFR 1.16 associated with this communication or credit any overpayment to Deposit Account No. 03-0678.

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